Bovine Serum – Session V

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VCS 2004, Rockville, USA

The regulation of serum

Viral safety

Tissue and cell development

‘Tissue’ culture ~100 years ago

Use of

ascitic fluid, blood, lymph clots, plasma clots, embryo extracts

Tissue and cell development

‘Cell’ culture ~50/60 years ago

Defined media + a natural extract

e.g. plasma clots, serum, embryo extracts

Serum:

protease inhibitors, adhesion factors, growth factors essential nutrients, hormones.

Serum and its use

- Bovine:

  foetal, newborn calf, calf, adult, donor
- Horse
- Porcine

- Vaccines
- Hybridomas
- Biotech, eg CHO cells

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USDA 9CFR 113.53

Requirements for ingredients of *animal* origin used for production of biologics

Each lot of material to be tested (if not sterilised)

a) free of mycoplasma

b) free of bacteria and fungi

c) test for viruses

USDA 9CFR 113.53

Viral testing

- Vero cells
- 1^{Y} cells / cell line bovine origin

Cells subcultured ≥2 times, for ≥21 days then tested for

- cytopathic agents
- hemadsorbing agents
- specified viruses by FAb tests

Requirements for testing subcultures

113.46

Detection of cytopathogenic and/or hemadsorbing agents.

General methods discussed

113.47

Detection of extraneous viruses by the fluorescent antibody technique

For bovine, canine, equine, feline, porcine materials

Fluorescent antibody technique 113.47

All cells tested for:

- BVDV
- Reo
- Rabies

Bovine cells tested for:

- Bluetongue
- Bovine adenovirus
- Bovine parvovirus
- Bovine RSV

Trypsin

Also regulated by CFR113.53

Specific test for PPV
(if not treated to inactivate PPV)

European Regulations

Eudralex

Volume 7B - Immunologicals:

table of extraneous agents to be considered

PharmEuropa

European Regulations

- Committee for Veterinary Medicinal Products
  CVMP
- Committee for Proprietary Medicinal Products
  CPMP
  (Now CHMP)
- PharmEuropa

CVMP

NfG on Requirements and control applied to bovine serum (foetal or calf) used in the production of immunological veterinary medicinal products

- Specified viruses: similar to CFR 113.47
- No viruses ultimately detected
- BVDV: test before/after inactivation
- Issues with BVDV antibodies

CPMP

NfG on the use of bovine serum in the manufacture of human biological medicinal products

- Generally, if contaminant detected, serum should not be used
- Specified viruses: similar to CFR 113.47
- But: encouraged to assess *Bovine polyoma*

Ph. Eur.

DRAFT Monograph on Bovine Serum

Specified viruses

- as for CFR 113.47
- *PLUS* bov. herpes 2, bov. herpes 4
- (also, BLV in donor herds)
- no evidence of viral contamination

Other regulations

- Japanese Pharmacopoeia, 14th edition – general viral safety of biotech/biologicals

- EC DG Sanco/C3/AH/R21/2000

  Scientific Committee on Animal Health and Animal Welfare

  Virus inactivation of bovine blood and blood products

  - inactivation recommended

Summary

Some discrepancies in guidance

- CPMP – BPyV
- *Draft* Ph.Eur. – BHV 2 & 4, BLV

Other

- CVMP - BVDV Abs

Other viruses of potential concern

Bovine herpes types ?

Bovine leukaemia?

Bovine circo?

Cache Valley?

Porcine circo?

Conclusions

Risk analysis as viral infection will invariably be present

- ability to grow on cell being used
- titre
- sensitivity to irradiation